Tissue Engineered Recellularized Laryngotracheal Implants

Grant Award Details

Tissue Engineered Recellularized Laryngotracheal Implants

Grant Type: Disease Team Therapy Development III

Grant Number: DR3-07281

Project Objective: The objective of this award is to achieve an IND filing with the FDA for an engineered trachea construct, using decellularized donor trachea repopulated with airway epithelial cells and MSCs to treat tracheal defects. They will develop an analogous product using rhesus monkey material and perform in vivo NHP studies to support their IND filing in preparation for a human clinical trial.

Investigator:

Name:	Peter Belafsky
Institution:	University of California, Davis
Type:	PI

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Name:	Alice Tarantal
Institution:	University of California, Davis
Type:	Co-PI

Disease Focus: Respiratory Disorders

Human Stem Cell Use: Adult Stem Cell

Award Value: $3,181,162

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3 (NCE)

View Report

Grant Application Details

Application Title: Tissue Engineered Recellularized Laryngotracheal Implants

Public Abstract: The goal is to bring a safe and effective therapy to adult patients with critical narrowing of the upper windpipe (trachea) and lower voicebox (larynx). Our intent is to implement all of the necessary steps for a successful new stem/progenitor cell-derived airway transplant for later stage clinical trials and/or commercialization within 4 years. Our team builds on first-in-human surgical successes with stem cell-based tissue engineered airway implants in compassionate use cases in adults and children. To this end, we will perform the necessary preclinical studies to support a successful IND application within 2 years, followed by a Phase I trial in 10 patients with 1 year of follow-up. We propose to use stem/progenitor cells from the patients themselves to treat an extraordinarily difficult to manage health problem, namely large airway stenosis. This causes severe airway obstruction, which severely limits quality of life, exercise tolerance, communication, and social and employment opportunities. Occasionally, the stenosis may also be life threatening. It occurs in approximately 200 individuals in California each year. Treatment costs for these patients are very high, and the personal and societal investments are substantially higher, although outcomes are consistently poor. The endpoint desired is normal airway and lung function and an improved quality of life. Our team aims to eliminate the need for repeated surgical interventions and/or the use of stents (metal or plastic tube implants), which are not necessarily successful, yet presently the standard of care for such patients.

In 2008/2010, we used stem cell-based, engineered tracheal implants to successfully save a young woman's and a child's life. Both are very well at 5 and 3 years post-implantation. These first-in-human studies emphasize that our goal is realistic, but also highlighted the gaps in our knowledge. Specifically, there is a need for preclinical studies to address questions of safety and long-term maintenance of airway, as well as to determine the fate of the implanted cells; secondly, if supported by these preclinical safety studies, there is a need for a formal clinical trial in patients of our candidate airway implant. Stem/progenitor cell-derived airway transplants that use the patients' own cells have the clinical advantage of not requiring anti-rejection medications. Our experience, to date, indicates such medication is not needed and this finding represents a scientific and clinical breakthrough in organ transplantation. While medical benefit was demonstrated in these two preliminary patients, there is substantial work to be done before such transplants can be considered routine for patients. We address this challenge with our team approach and emphasize the synergism that occurs when linking team members from California and a partner institution, with expertise in a variety of scientific and medical disciplines to address this critical need.

Statement of Benefit to California:	The citizens of California have generously invested in stem cell research and a return on their investment will include breakthroughs in medical treatments for diseases where there are currently limited options. Tissue-engineered stem/progenitor cell-derived airway transplantation is a leading example of translational research in regenerative medicine that can be used for a host of diseases. Through this team effort scientists and physicians will lead the early promise of airway transplantation to clinical trials in California and beyond. This research team proposes to use tissue-engineered airway scaffolds with stem and progenitor cells to cure an extraordinarily difficult to manage and life-threatening health problem. Severe airway obstruction occurs in approximately 200 adults in California each year. The morbidity associated with this disease is very high, and it can be fatal for some. The knowledge gained from the tissue engineering and preclinical studies proposed will provide a new technology that can be applied to these and other disorders in California. We foresee that our stem cell-derived airway transplant could also be extended to treat an important subpopulation of children with severe subglottic and tracheal stenosis, malacia, or agenesis that have proven refractory to standard surgical interventions, and adult patients with debilitating laryngeal scarring. A further exciting possibility is that stem cell-derived airway transplants or bioengineered stents could also be applied to treat an important subpopulation of adults with severe chronic obstructive pulmonary disease (COPD). Given that the prevalence rate of COPD for California citizens greater than 65 years of age approaches 10%, if even 0.1% of COPD patients in California were candidates, specifically those with associated tracheobronchomalacia, then greater than 3,000 patients might benefit from this treatment. The methods and technology developed from this project can also be used as the basis for other similar health needs including esophageal, bladder, and bowel replacements for disorders where present treatments are very limited and impair quality of life.